

Polish Society of Gynecologists and Obstetricians Guidelines for the application of hysteroscopy in gynecology

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This guideline presents current management recommendations which may be modified and altered in justifiable cases, after careful analysis of a given clinical case, which in the future might constitute grounds for modification and updating.

OBJECTIVES

The objective of this guideline is to present up-to-date knowledge about the application of hysteroscopy in gynecology, based on the experience of the authors and reliable sources from the literature.

INTRODUCTION

Hysteroscopy is a minimally invasive procedure which is performed to diagnose and treat diseases of the uterine cavity and the cervical canal. The two types of the procedure include diagnostic and operative hysteroscopy. Diagnostic hysteroscopy allows for a direct visualization of the cervical canal, uterine cavity and tubal ostia and, if necessary, a targeted biopsy. Operative hysteroscopy facilitates intrauterine and/or intracervical lesion excision using mechanical or electrosurgical resection methods as well as laser techniques. Due to technological advances and miniaturization of the hysteroscopic tools, the number of diagnostic hysteroscopies with simultaneous excision of the lesions (the so-called 'see-and-treat' hysteroscopy) is steadily increasing [1, 2].

Hysteroscopy is a safe procedure and is well-tolerated by the patients [3].

INDICATIONS FOR HYSTEROSCOPY

Due to the wide range of possible applications of uterine cavity and cervical canal imaging, the list of indications for hysteroscopy continues to expand. Also, hysteroscopy allows to collect tissue samples, when necessary.

The indications for hysteroscopy include [3–7]:

- Abnormal uterine bleeding in reproductive age women;
- Post-menopausal bleeding;
- Suspicion of endometrial hyperplasia and other endometrial pathologies (endometrial polyps, diagnostic process for endometrial hyperplasia and endometrial cancer);
- Corroboration of histopathology results;
- Suspicion of submucosal or intramural fibroids;
- Suspicion of congenital uterine anomaly;
- Suspicion of intrauterine adhesions;
- Corroboration of ultrasound diagnosis of uterine abnormalities;
- Repositioning and/or removal of an intrauterine device or other foreign bodies from the uterine cavity;
- Suspicion of retained products of conception;
- Suspicion of lesions within the cervical canal;
- Part of the diagnostic process for infertility and/or recurrent miscarriage;

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- Endometrial ablation/resection;
- Vaginoscopy (e.g. removal of a foreign body from the vagina in young girls – *virgo*).

Indications for hysteroscopy may also include clinical situations in which uterine cavity, cervical canal and tubal ostia imaging is vital for the diagnostic and therapeutic management of the affected patients, e.g. treatment of symptomatic niche in the cesarean section scar, injection of methotrexate or other pharmacological agents into the gestational sac located in the cesarean section scar, diagnostic and/or operative hysteroscopy, with or without biopsy, before operative procedures in gynecology [8, 9].

In case of suspicion of intrauterine lesions, hysteroscopy is used during the diagnostic process for infertility, recurrent miscarriage or before assisted reproductive techniques (ART). At present, hysteroscopy is not routinely recommended in the diagnosis of infertility or before IVF procedures if ultrasonographic appearance of the uterus is normal [10–13].

CONTRAINDICATIONS TO HYSTEROSCOPY

Absolute contraindications to hysteroscopy include [3, 14]:

- suspected or diagnosed normal viable intrauterine pregnancy;
- active infection of the genital organs, including herpes simplex of the genital area;
- cervical cancer.

Relative contraindications to hysteroscopy include:

- excessive uterine bleeding;
- severe systemic disease.

Bleeding from the genital tract is not an absolute contraindication to hysteroscopy but obstructed visualization of the intrauterine structures may be expected. In such cases, it is necessary to select adequate instruments (flow hysteroscope with proper diameter and isoosmotic medium) [15].

INSTRUMENTS

Types of hysteroscopes

Both, for the operative and diagnostic hysteroscopy, the type of the hysteroscope should be adjusted to the type of the procedure and operator's experience, as well as modified to the intraoperative conditions [4, 16, 17]. It is advisable to use a hysteroscope with the smallest possible diameter of the sheath, individually tailored to the needs of the patient, and allowing for optimal visualization and least traumatic procedure [3, 4, 18].

Media types

Visualization of the intrauterine structures requires distension of the uterine cavity using medium agents. The choice of the distending medium for hysteroscopy is at the discretion of the operator. At present, the 0.9% sodium

chloride (NaCl) is the liquid medium of choice for diagnostic hysteroscopy [3, 18, 19]. Other than in exceptional situations, a gaseous medium — carbon dioxide (CO₂) — is not advisable in order to avoid the presence of gas embolism [3]. Also, the use of 0.9% NaCl is associated with lower frequency of vasovagal syncope as compared to CO₂ [4]. A liquid medium, as opposed to gaseous one, allows to wash out the mucus and the blood from the uterine cavity, thus improving visualization and shortening the duration of the procedure [20, 21]. For operative hysteroscopy, only liquid media are used. Their advantage consists in washing out the tissue fragments and blood which occur during intrauterine lesion excision, thus obtaining adequate view of the uterine cavity during the procedure [18–20].

Liquid media are subcategorized into:

- non-electrolyte dissension media (5% mannitol, 3% sorbitol, and 1.5% glycine) and
- isotonic electrolyte-containing media (0.9% sodium chloride, Ringer's solution).

As for electric conductivity, non-electrolyte dissension media are nonconductive, so they are used during procedures with monopolar electrodes [3, 18]. On the downside, they are hypotonic. In the event of excessive absorption into the circulatory system, they may lead to fluid overload, hyponatremia, and lowered plasma osmolarity, which might result in cerebral edema or even death [3, 18, 22]. Electrolyte-containing media are electrically conductive and cannot be used for procedures with monopolar electrodes [3, 18–20]. They are, however, the medium of choice for operative hysteroscopy with bipolar electrodes [3, 18]. Their isotonicity is their primary advantage, as they reduce the risk for hyponatremia and lowered plasma osmolarity.

BEST PRACTICE IN HYSTEROSCOPY

Eligibility criteria

Patients are deemed eligible for the procedure on the basis of the pelvic exam and medical history. Additionally, an ultrasonographic examination should be performed, using transvaginal probe, if possible. In justified cases, additional imaging methods (*i.e.* sonohysterography and nuclear magnetic resonance) may also be applied during patient eligibility check. The abovementioned methods, unlike hysteroscopy, allow for the assessment of the myometrium and the external uterine contour. Additional imaging methods, especially transabdominal or transrectal ultrasound, and sometimes laparoscopy, can be used intraoperatively and may increase both, safety and effectiveness of some advanced hysteroscopic procedures [23–25].

Informed consent

Written informed consent must always be obtained before every hysteroscopic procedure. It is necessary to

discuss the following with the patient: hysteroscopy type, benefits and risk related to the procedure, and alternative methods of management.

Timing of the procedure

For menstruating women, the first phase of the cycle, immediately after the bleeding ceases, is the optimal time to carry out the procedure, as the endometrium in the early proliferative phase is thin and allows for a better visualization of the intrauterine structures and possible pathologies [3]. In the secretory phase, thickened endometrium may impede imaging and visualization, thus increasing the risk for misdiagnosis (underdiagnosis of small lesions and overdiagnosis of endometrial polyps).

In post-menopausal women, hysteroscopy may be performed at any given time.

Cervical preparation

Difficulty in inserting the hysteroscope through the cervical canal into the uterine cavity is among the main causes for unsuccessful hysteroscopy and is responsible for approximately 50% of the related complications [4, 26]. Therefore, in selected cases of operative hysteroscopy, pharmacological preparation of the cervix using misoprostol (vaginally, 200–400 µg) is allowed [3, 4, 27–30]. Randomized studies found no proof of increased number of successful procedures or lowered risk for complications or pain reduction for diagnostic hysteroscopy [27–29, 31]. Thus, routine use of misoprostol for cervical preparation before diagnostic hysteroscopy is not recommended [4].

Notably, the use of misoprostol for cervical preparation is an off-label approach.

In cases of cervical stenosis, osmotic distending media, intraoperative ultrasound, vaginoscopic approach, manual dilation and hysteroscopic dissection of the stenotic cervical canal may be also applied [26, 32].

Endometrial preparation

Pre-operative administration of the endometrial thinning agents may be considered in women undergoing elective operative hysteroscopy (e.g. uterine septum resection, submucosal fibroid resection, endometrial ablation) to ensure a better view during the procedure [33]. Such management is not recommended for diagnostic hysteroscopy as it might affect the histopathology results.

Vaginal preparation

After excluding the contraindications to hysteroscopy (like active inflammation of the genital organs), vaginal discharge ought to be examined before the procedure. If no signs of inflammation are present, hysteroscopy may be conducted. Culture of the cervix is not routinely required.

It is advisable to visualize the vaginal portion of the cervix using the speculum and wash the vagina and the vaginal portion with an antiseptic solution suitable for mucous membranes. Vaginoscopic approach (i.e. the so-called 'no touch' technique) is also allowed [4, 34, 35]. It consists in insertion of the hysteroscope into the vagina, through the cervical canal and into the uterine cavity without the use of a speculum or cervical instrumentation. Vaginoscopic approach is recommended in situations when it is difficult or impossible to insert a speculum. The procedure may be conducted without the need to disinfect the vagina if vaginal discharge is normal.

Settings

Advances in technology and increasing miniaturization of the hysteroscopes allow to conduct diagnostic and simple operative hysteroscopies in outpatient settings [4, 36, 37]. The decision between outpatient and hospital setting should be made with caution.

Hospital settings should be recommended to patients with: [3, 38]:

- intrauterine lesions which require advanced operative procedures;
- cervical stenosis or atresia;
- concomitant diseases which elevate the risk for complications;
- limited uterine maneuverability;
- no tolerance of local anesthesia.

In the remaining cases, ambulatory settings may be recommended to patients.

Elimination of perioperative pain

Hysteroscopy-related pain remains to be one of the main limitations for a successful procedure in ambulatory settings, so it is vital to be familiar with techniques of pain reduction [38, 39]. Friendly atmosphere and engaging the patient in a conversation play a significant role in reducing pain and anxiety associated with the procedure [40]. Depending on the emotional condition of the patient and her attitude, anesthesia is not necessary during a diagnostic hysteroscopy in most women [41, 42]. The benefits of avoiding anesthesia include shortened time of the procedure and no adverse effects, especially no pain associated with paracervical block [41].

Also, small-diameter sheath hysteroscopes are key elements in pain reduction. Randomized studies revealed that the use of hysteroscopes with sheath diameter less than 4 mm correlates with significantly less pain as compared to the use of higher diameter hysteroscopes with simultaneous paracervical block [43].

Opioids reduce pain during and after the procedure, but caution is advised due to possible adverse effects [4, 44].

Non-steroidal anti-inflammatory agents (NSAIDs) do not relieve the pain during hysteroscopy but significantly reduce it after the procedure [4, 45]. Local anesthetics, *e.g.* lidocaine spray on the vaginal portion of the cervix, is not an effective means of pain relief during hysteroscopy [46]. Likewise, lidocaine and mepivacaine administration into the cervical canal proved ineffective [46].

Paracervical block using lidocaine or mepivacaine reduces pain associated with cervical dilation and endometrial biopsy, and lowers the risk for severe pain during hysteroscopy [47], so it should be considered in cases when cervical dilation is necessary or when intrauterine lesions are to be removed [4, 47].

Sedation, regional or general anesthesia should not be used in ambulatory settings as they require strict monitoring of the vital signs and are connected with possible complications [48]. They should only be administered in setting where adequate anesthesiological standards are maintained.

HYSTEROSCOPIC BIOPSY

Hysteroscopic endometrial biopsy should replace diagnostic curettage of the uterine cavity [49]. Sensitivity of the hysteroscopic endometrial biopsy is significantly higher, especially in case of focal lesions. Diagnostic curettage of the uterine cavity, if conducted as a sole diagnostic procedure, is not sufficient for full diagnostics of the endometrium in case of focal lesions [50, 51]. Therefore, hysteroscopy and targeted biopsy should be considered in women with indications for histopathological examination of the endometrium (*e.g.* in the diagnosis of endometrial cancer) [51, 52]. It makes it possible to collect focal lesions, which might otherwise be omitted during blind biopsy or curettage, for evaluation [51, 52]. In case of extensive suspicious changes in the uterine cavity, subsequent curettage is allowed.

It is not always possible to obtain enough endometrial tissue for histopathologic evaluation, especially in postmenopausal women with endometrial atrophy [53–55]. In a meta-analysis of studies on endometrial biopsy, non-diagnostic histopathology results were found in as many as 54% of the women with post-menopausal bleeding [54]. According to reliable reports in the literature, results of imaging studies are sufficient to plan further management in case of patients with non-diagnostic histopathology results [53–55]. If hysteroscopy confirmed atrophic endometrium and histopathology results are non-diagnostic, repeat biopsy is not necessary, unless new indications are present [53–55].

Risk for tumor cell dissemination in the peritoneal cavity

Hysteroscopy is associated with a certain risk for tumor cell dissemination into the peritoneal cavity due to the passage of the medium through the fallopian tubes. The available data are not conclusive with regard to a possi-

ble increase in the incidence of positive peritoneal cytology after the use of hysteroscopy in the diagnosis of endometrial cancer. So far, various meta-analyses have found a link between the use of liquid media and higher incidence of positive peritoneal cytology, but no relationship between potential tumor cell dissemination and disease progression was detected [56–61].

In order to reduce the risk for cell dissemination in cases of suspected endometrial cancer, it is advisable to use the lowest possible pressure of the distending medium, preferably not exceeding 50 mmHg. In a study using saline solution and intrauterine pressure of 25–50 mmHg, the authors found that hysteroscopy did not increase the risk for microscopic intraperitoneal tumor cell dissemination as compared to curettage [62]. More prospective studies in that area are necessary.

COMPLICATIONS OF HYSTEROSCOPY AND THEIR PREVENTION

Early complications:

- uterine perforation;
- heavy bleeding;
- absorption of the distending medium;
- gas embolism;
- fluid overload.

Late complications:

- iatrogenic adhesions after hysteroscopy;
- pelvic inflammatory disease.

Uterine perforation

The incidence of uterine perforation during diagnostic and operative hysteroscopy has been estimated at 0.13% and 0.5–3%, respectively [62, 63]. Perforation may occur either during the attempt to enter the uterine cavity or intraoperatively, during lesion excision. Risk factors for perforation during hysteroscope insertion include [4, 63]:

- cervical stenosis and the need for cervical dilation (as a result of atrophy, previous surgery, or no previous vaginal delivery);
- torsion of the cervical canal and uterine cavity (frequently occurs in case of fibroids and pelvic adhesions).

The highest risk for uterine perforation is associated with the excision of massive intrauterine adhesions [63]. Should perforation occur, it is possible to either monitor the patient or consider performing laparoscopy or laparotomy to stop the bleeding and assess for possible intestine or bladder trauma [3]. Assessment of the bowel and the bladder is necessary in the event of uterine perforation using an electrosurgical tool or laser due to the risk for thermal injury [64]. Suturing of the uterine perforation is advised in reproductive age women to prevent a possible uterine scar rupture during subsequent pregnancy [65]. It is important

to bear in mind that if the perforation is localized within the cervix or the lateral uterine wall, it may cause bleeding into the retroperitoneal space [3].

If fundal perforation occurs while using a thin hysteroscope, a thin Hegar device, or an uterine probe in a post-menopausal woman without signs of bleeding into the abdominal cavity, it is possible to simply monitor the patient. Detailed imaging to exclude bleeding into the abdominal cavity and a 24-hour monitoring at a postoperative care unit are necessary. Should patient clinical and laboratory (complete blood count, C-reactive protein) parameters remain stable after 24 hours, the perforation may be diagnosed as non-symptomatic and not requiring surgical intervention.

In cases when hysteroscopic entry is difficult, it is advisable to establish the path of the cervical canal and its relation to the uterine axis before 'blind' cervical dilation [3, 26]. For that purpose, a small-diameter flexible or rigid hysteroscope may be used, which allows for visual control during dilation of the cervical canal with the tip of the hysteroscope or microtools inserted through the operative channel [26]. Uterine probe, bimanual examination, transvaginal, transrectal or transabdominal ultrasound are also useful while attempting to establish the path of the cervical canal and its relation to the uterine cavity. Difficulty with hysteroscopic entry into the uterine cavity may be reduced by cervical preparation with misoprostol [29].

Hemorrhage

Clinically significant bleeding during diagnostic hysteroscopy is rare and is usually associated with uterine perforation. The incidence of clinically significant bleeding related to operative hysteroscopy has been estimated at 0.61% [63]. Apart from uterine perforation, other causes for bleeding include cervical trauma, bleeding at the operation site or bleeding diathesis.

In the event of intraoperative bleeding, coagulation using mono- and bipolar electrodes may be applied (the choice of the electrodes depends on the medium used during the procedure).

Postoperative bleeding from the uterine cavity may be stopped by using uterotonics, antifibrinolytics, or balloon tamponade (e.g. using a Foley's catheter).

If none of the above methods proved sufficient, it may be necessary to perform uterine artery embolization or hysterectomy. The patient should be made aware of that risk and information about a possible hysterectomy should be included in the informed consent for all hysteroscopic procedures [3, 63].

Embolism

Air embolism may occur during hysteroscopy using either gaseous medium — CO₂ or liquid medium, as air

bubbles are present in the liquid medium as well [18, 66]. The symptoms include dyspnea, chest pain, tachycardia, anxiety, sudden hypotension and hypoxemia [18]. Vascular access and a pressure gradient are necessary for CO₂ or air to get into the cardiovascular system, and then to the right ventricle and to the pulmonary arteries [3]. Therefore, to avoid this complication, it is vital to keep the rate of the CO₂ flow below 100 mL/min., and the uterine cavity pressure below 100 mmHg [3]. Importantly, laparoscopic insufflators should not be used for hysteroscopic procedures as they have very high CO₂ flow rate [3]. Carbon dioxide should not be used during operative hysteroscopy due to the risk for CO₂ passage into the open vessels [18]. To avoid air passage into the uterine cavity during hysteroscopy with liquid medium, tubing and hysteroscopy channel ought to be flushed until all air bubbles are removed. Caution is also advised when bags containing liquid media are changed to avoid air entering tubing [3].

FLUID OVERLOAD

Operative hysteroscopy intravascular absorption syndrome (OHIA) occurs when a significant amount of the liquid medium is absorbed into the circulation [63, 67]. At present, the incidence of OHIA has been estimated at < 1% [18, 63, 68, 69]. The absorption occurs by the opened uterine veins as a result of pressure gradient (venous pressure: 10–15 mmHg, distending media pressure in the intrauterine cavity: 40–60 mmHg) [63]. Absorption of the distention media may also occur by peritoneal surface due to the retrograde passage of the fluid through the Fallopian tubes [18].

Risk factors for fluid overload include high (exceeding the mean blood pressure) pressure in the uterine cavity, prolonged duration of the procedure, and contact between the medium and the opened myometrial venous sinuses (mainly during electrosurgical fibroid resection or the resection of the endometrium) [70–72].

Massive absorption of a hypotonic medium (glycine, mannitol, sorbitol) leads to hyponatremia, which is manifested with headache, nausea, vomiting and fatigue. In case when sodium levels drop below < 120 mmol/L, lowered plasma osmolarity will lead to cerebral edema, including the risk for brain herniation [3, 28, 73].

Massive absorption of an isotonic medium (0.9% sodium chloride, Ringer's solution) will not cause electrolyte imbalance but may lead to hypervolemia with pulmonary edema and heart failure [3, 18].

In accordance with the international consensus, a fluid deficit (difference between the volume of fluid infused into the uterus and the volume of fluid evacuated from the uterus) should not exceed 1000 mL for hypotonic (glycine, mannitol, sorbitol) and 2500 mL for isotonic solutions. These thresholds apply to healthy reproductive age women [18].

In case of elderly women with renal and cardiovascular problems, the upper fluid deficit levels should be 750 mL and 1500 mL, respectively [19]. Therefore, careful monitoring of the fluid deficit during hysteroscopy is necessary. The procedure should be stopped when the fluid deficit is reaching the abovementioned limits or when the clinical symptoms of fluid overload occur. In order to lower the risk for hyponatremia and the related complications, iso-osmotic media such as 0.9% sodium chloride or Ringer's solution should be the preferred choice for operative hysteroscopy [18]. The information about fluid deficit should be included in the operation report.

Iatrogenic adhesions after hysteroscopy

Hysteroscopic resection of the intrauterine lesions is associated with significantly lower risk for *de novo* adhesion formation as compared to curettage [74]. Therefore, uterine curettage in order to obtain endometrial samples in women undergoing diagnosis for infertility should be avoided. The incidence of adhesion formation after operative hysteroscopy depends on the type of the procedure. Polypectomy is associated with the lowest and multiple submucosal fibroid resection with the highest risk for adhesion formation, respectively [74]. The following procedures may decrease the risk for intrauterine adhesion formation after hysteroscopy: avoidance of electrosurgical tools, early second-look hysteroscopy, estrogen therapy, intrauterine systems (IUD, balloon), stem cells, hyaluronic acid gels or carboxymethyl cellulose gels [74–76]. At present, we lack reliable data advocating routine use of any of the abovementioned methods of preventing adhesions after hysteroscopy [75].

Pelvic inflammatory disease

The incidence of inflammatory diseases after hysteroscopic procedures has been estimated at < 1%, so routine antibiotic prophylaxis is not required [77–79]. Guidelines on patient eligibility and preparation for the procedure, which constitute preventive measures for post-hysteroscopic inflammation, have been presented earlier in the text.

SUMMARY

The benefits of diagnostic hysteroscopy include direct visualization of the intrauterine structures and, when necessary, performing a minimally invasive targeted biopsy for histopathology evaluation.

Operative hysteroscopy allows for a minimally invasive excision of intrauterine lesions.

Hysteroscopy is well-tolerated and safe for the patients.

Hysteroscopy is the basis of the modern diagnostic process and the treatment of uterine diseases, and every effort should be made to increase its availability in Poland.

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